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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: August 25, 2010

SUBJECT: Tolerance Exemption Petition Review in Support of Tagetes Oil.

Decision Number: 420841
DP Number: 372967
EPA Petition Number: 9F7619
Chemical Class: Biochemical
PC Code: 176602
CAS Number: 8016-84-0
Active Ingredient Tolerance Exemptions: None
MRID Numbers: 47868201-47868237

FROM: Angela L. Gonzales, Biologist
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Colin Walsh, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

~~THE FOLLOWING CONTAINS CONFIDENTIAL BUSINESS INFORMATION~~

ACTION REQUESTED

On behalf of Plant Impact PLC., E[x]ponent, Inc. has submitted a tolerance exemption petition for the active ingredient, tagetes oil. The petition is in support of a proposed end-use product (EP), Bug Oil Food Use (EPA File Symbol No. 85937-E). The product is intended for use as an insecticide/acaricide for the control of mites, whiteflies, aphids, thrips, mealybugs, scales and pyslla on all food crops.

Executive Summary

The available information and data are insufficient to support the request for an exemption from the requirement of a tolerance for tea tree oil at this time.

RECOMMENDATIONS AND CONCLUSIONS

1. A risk assessment cannot be completed at this time to support a tolerance exemption due to gaps in the toxicology database for tagetes oil. Once these data requirements have been satisfied, the risk assessment will be completed. Refer to the memorandum from A. L. Gonzales to C. Walsh dated 8/25/10 for a discussion of these data gaps.

STUDY SUMMARIES

Chemical Identity and Uses of Tagetes Oil

Tagetes Oil is a new biochemical pesticide active ingredient intended for use to insecticide/acaricide for the control of mites, whiteflies, aphids, thrips, mealybugs, scales and pyslla on horticultural and agricultural crops. It appears that the active ingredient is extracted from the flowering herb, *Tagetes minuta* (Muster John Henry or Mexican Marigold) but this must be verified by the registrant. There are many species within the *Tagetes* genus. The herb is non-native to the United States, but is found in California, Hawaii and in most of the states on the east coast (USDA Plants Database, 2010). It has a widespread geographic distribution but is prevalent in subtropical and tropical climates. The major constituents of the identified components of tagetes oil are terpenes, which are found in a variety of essential oils.

Tagetes oil, as *Tagetes patula L.*, *T. erecta L.*, or *T. minuta L.* (*T. glandulifera* Schrank) is approved for use in food as a natural flavoring substance and natural adjuvant (in the oil form only) under 21 CFR 172.510. The ingredient is used in some cosmetics including shampoos, soaps and lotions (EWG, 2010).

Toxicological Profile of Tagetes Oil and Hazard Assessment

The data presented in Table 1 below are a summary of the toxicity data and information submitted for tagetes oil. At this time, all data requirements have been adequately satisfied with the exception of acute inhalation toxicity, 90-day oral toxicity, 90-day inhalation toxicity, developmental toxicity and mutagenicity.

Table 1. Mammalian Toxicology Data Requirements for Tagetes Oil (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} >5,000 mg/kg (females)	IV	47868213
Acute dermal toxicity (rats) (870.1200)	LD_{50} >2000 mg/kg for males, females, and for both sexes combined	III	47868214
Acute inhalation toxicity (870.1300)	**Information to support data requirement is inadequate.** Rationale based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in product. This is not enough information to indicate a lack of toxicity. The potential for exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists.		47868208
Primary eye irritation (870.2400)	Minimally irritating: positive conjunctival irritation and moderate reddening of sclerae were noted on 3/3 rabbits one hour post-instillation with clearance by 24 hours.	IV	47868215
Primary dermal irritation (rabbit) (870.2500)	Moderately irritating: well defined erythema on 3/3 rabbits one hour after patch removal with clearance on one rabbit by day 7, with reduction to very slight erythema on the second rabbit by 72 hours and clearance by day 7, and with reduction to very slight erythema on the third rabbit by day 7 and clearance by day 10. Very slight edema on 3/3 rabbits one hour after patch removal with clearance by 24 hours. Scaling on all rabbits on day 7 with clearance on two rabbits by day 14 and persistence on one rabbit through day 14.	III	47868216
Dermal sensitization (guinea pig) (870.2600)	Not a sensitizer. No positive signs of reactivity at 24 and 48 hours after challenge in test and naïve control animals after three consecutive weekly inductions.		47868217
Hypersensitivity incidents (885.3400)	Any incidents must be reported		
90-Day oral toxicity (870.3100)	**Information to support data requirement is inadequate.** Rationale based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in product. Additional information submitted on individual components tagetes oil. This is not enough information to indicate a lack of toxicity. The potential for dietary exposure to the active ingredient exists.		47868218
90-Day dermal toxicity (870.3250)	Waived: prolonged dermal exposure not anticipated based on use pattern (no purposeful application to the skin) and appropriate PPE requirements on label.		

Table 1. Mammalian Toxicology Data Requirements for Tagetes Oil (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
90-Day inhalation toxicity (870.3465)	**Information to support data requirement is inadequate.** Rationale submitted for acute inhalation based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in product. This is not enough information to indicate a lack of toxicity. The potential for repeated exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists.		
Mutagenicity (870.5100, 5300 and 5375)	**Information to support data requirement is inadequate.** Rationale based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in product. Additional information submitted on individual components tagetes oil. This is not enough information to indicate a lack of toxicity. The potential for dietary and inhalation exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists.		47868213
Developmental toxicity (870.3700)	**Information to support data requirement is inadequate.** Rationale based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in product. Additional information submitted on individual components tagetes oil. This is not enough information to indicate a lack of toxicity. The potential for dietary and inhalation exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists.		47868213

90-day Oral

A 90-day oral study was not submitted. Based on the available information, the potential for dietary exposure to residues of tagetes oil exists. Although the registrant states that the active ingredient is used in herbal medicines, aromatherapy and as a flavoring in foodstuffs, this is not enough information to indicate a lack of toxicity. An absence of reported toxicity in the literature does not indicate an absence of toxicity. Some toxicology data have been submitted on the individual components of tagetes oil (specifically *d*-limonene) to support the data requirements. These data are inadequate to satisfy the data requirements because they do not represent the oil itself. Toxicity cannot be ascertained for tagetes oil based on toxicity data on one or some of its components. Data on individual components may not be bridged to satisfy data requirements for tagetes oil. An assessment must be made regarding the potential for toxicity from dietary exposure to tagetes oil through pesticidal use. Due to the lack of subchronic or chronic oral toxicity data, it cannot be determined if dietary exposure to tagetes oil from the proposed uses would result in toxicological effects.

90-Day Dermal and 90-Day Inhalation

A 90-day dermal study was not submitted and is not required at this time for the use of tagetes oil in the proposed EP, Bug Oil Ornamental. Prolonged exposure via the dermal route is not anticipated because the product is not purposely applied to the skin and handlers/applicators are required to wear appropriate PPE.

Information was provided to support the 90-day inhalation data requirement but is inadequate. The rationale submitted for acute inhalation was based on presence in foodstuffs, perfumes and in herbal and aromatherapy and low concentration in the proposed product. This is not enough information to indicate a lack of toxicity. The potential for repeated exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists. There are no PPE requirements regarding mitigation of inhalation exposure on the proposed EP label. Refer to the DERs for more information.

Prenatal Developmental and Mutagenicity

The information provided to support the developmental toxicity and mutagenicity data requirement is substantially similar to the rational provided to support the 90-day oral and 90-day inhalation data requirements, but is inadequate. Some toxicology data have been submitted on the individual components of tagetes oil (specifically *d*-limonene) to support the data requirements. These data are inadequate to satisfy the data requirements because they do not represent the oil itself. Toxicity cannot be ascertained for tagetes oil based on toxicity data on one or some of its components. Data on individual components may not be bridged to satisfy data requirements for tagetes oil. The potential for dietary and inhalation exposure exists (see above); therefore, repeat exposure is possible. There are no PPE requirements regarding mitigation of inhalation exposure on the proposed EP label. It is unknown if exposure to the active ingredient via the dietary or inhalation route would result in developmental, reproductive and/or mutagenic effects. Refer to the DERs for more information.

Effects on the Endocrine System

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Tagetes oil is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit the website: http://www.epa.gov/endo/.

Exposure Assessment

Dietary Exposure-Food

Refer to the Chemical Identity and Uses of Tagetes Oil section above for information regarding current uses and occurrence of tagetes oil.

Dietary exposure may occur based on the pesticidal use pattern. Tagetes oil will be applied directly onto a variety of growing food crops. A dietary exposure and risk assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

Dietary Exposure-Drinking Water

Once all physical and chemical properties data requirements are satisfied, the drinking water exposure assessment will be conducted.

Non-Dietary Exposure-Dermal and Inhalation Exposure

Prolonged exposure via the dermal route is not anticipated because the product is not purposely applied to the skin and handlers/applicators are required to wear appropriate PPE.

Exposure via the inhalation route is anticipated for handlers/applicators. The potential for repeated exposure to the concentrated product (the AI is volatile) and the diluted product as a spray exists. There are no PPE requirements regarding mitigation of inhalation exposure on the proposed EP label.

Occupational Exposure and Risk Assessment

An occupational exposure assessment will be conducted once the acute inhalation, 90-day inhalation, developmental toxicity and mutagenicity data requirements have been satisfied.

Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

A dietary exposure and risk assessment will be conducted once all mammalian toxicology data requirements have been satisfied.

Aggregate Exposure

The aggregate exposure assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

Cumulative Effects

Cumulative effects will be assessed once all product chemistry and mammalian toxicology data requirements have been satisfied.

Risk Characterization

The risk assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

REFERENCES

Environmental Working Group (EWG) Database. 2010. Products Containing *Tagetes* Oil. http://www.cosmeticsdatabase.com.

USDA Plants Database. 2010. *Tagetes minuta.* U.S. Department of Agriculture Natural Resources Conservation Service. http://plants.usda.gov/java/profile?symbol=TAMI3 June 29, 2010.

cc: A. L. Gonzales, C. Walsh, BPPD Science Review File, IHAD/ARS
A. L. Gonzales, FT, PY-S: 8/25/10

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Chemical Name: Oils, Tagetes

PC Code: 176602
HED File Code: 41500 BPPD Tox/Chem
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Accession #: 000-00-0136

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